Interstitial Laser Coagulation: Evaluation of the Effect of Normal Liver Blood Perfusion and the Application Mode on Lesion Size

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Background and Objective: **The effect of temporarily interrupted hepatic blood flow and multiple-fiber application on necrosis volume in interstitial laser coagulation (ILC) was investigated.**
Study Design/Materials and Methods: **Single- and multiple-fiber ILC were performed in porcine livers with normal as well as interrupted perfusion. Temperatures were determined. Lesions were measured and studied by light microscopy 4 hours post-treatment.**
Results: **ILC with multiple-fiber application led to significantly greater individual lesion volumes (3.7 ± 0.5 cm³) than single-fiber application (2.5 ± 0.5 cm³) ($P < .01$). The interruption of hepatic perfusion led to a significant increase in lesion volume with single- (7.5 ± 1.0 cm³) as well as multiple-fiber application (12.6 ± 2.2 cm³) ($P < .01$). Superposition of the lesions in the multiple-fiber application mode was only determined with interrupted perfusion (total volume: 50.3 ± 6.6 cm³).**
Conclusion: **Interruption of hepatic perfusion increases lesion volumes significantly. ILC for treating liver tumors should preferably be performed by application routes that permit temporary interruption of hepatic perfusion. Lasers Surg. Med. 23:40–47, 1998.**

Key words: ILC; LITT; hepatic perfusion; interstitial laser coagulation; liver surgery; liver tumors; multiple-fiber application; single-fiber application

INTRODUCTION

Differential clinical and experimental studies have shown that interstitial laser coagulation (ILC), first described by Bown in 1983 [1], can be done percutaneously by laparoscopy or laparotomy for the treatment of malignant liver tumors [2–5]. ILC is a method in which laser fibers are directly inserted into the tumor tissue for inducing local thermal therapy. The purpose of this in situ ablation technique is to locally destroy tumor tissue with maximum protection of surrounding healthy tissue and to avoid extensive surgical resections [6,7]. Hyperthermia (42–45°C) as well as direct tissue coagulation (60–140°C) occur in ILC, but temperatures leading to tissue carbonization (300–1,000°C) have to be avoided because of the resultant impairment of heat conduction [8,9].

Broad clinical application of ILC is still lim-

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ited by the small size of inducible tumor destruction. In view of the oncologically required safety margin of healthy liver tissue, the currently attainable necroses are not extensive enough for treating larger human liver tumors. The size of the heated region generally depends on the optical wavelength, applicator system, power and time protocol, thermal tissue properties, and the blood perfusion rate [10]. In an experimental study Steger et al. induced lesion volumes of 10 cm^3 using a multiple-fiber application system which allowed the simultaneous application of four bare quartz fibers [11]. That way, Steger et al. showed the importance of the application mode with respect to the coagulation volume.

The blood perfusion rate becomes an important parameter in highly perfused organs such as the liver [12]. From a physiological point of view, precise estimation of the perfusion rate is a difficult task because there are wide inter- and intraindividual variations [13–15]. On the other hand, blood exchange may have such high values that the temperature distribution will strongly be influenced due to the cooling effect. The heat loss will be additionally increased if larger vessels are located near the laser source. This was clearly shown by Matthewson et al. who found a significant temperature decrease and a less marked tissue effect during laser-induced thermotherapy in the area of larger hepatic blood vessels [16]. It thus appears to be important for the success of the therapy to interrupt blood perfusion in organs with a high perfusion rate in order to enlarge the coagulation zone. The special anatomy of the vascular supply to the liver allows complete interruption of hepatic blood flow by occlusion of the hepatoduodenal ligament.

The aim of this experimental study was to investigate the effect of temporary interrupted hepatic blood flow on necrosis volume in ILC. For this purpose, single- and multiple-fiber applications were performed in normal pig livers with maintained as well as interrupted liver perfusion. We monitored the tissue temperatures during the application and measured the volumes of tissue coagulation induced by a total power of 5 W at each fiber and an exposure time of 840 sec.

MATERIALS AND METHODS

A Nd:YAG laser (Dornier-Medizintechnik, Munich, Germany) with a wavelength of 1,064 nm was used in continuous wave mode to induce interstitial laser coagulation. For multiple-fiber laser applications we applied a beam-splitter with a special optical coupling which permits the simultaneous use of four fibers (Dornier-Medizintechnik, Munich, Germany). Each of the four 600-μm quartz fibers had a 25-mm Ringmode®-ITT applicator (Dornier-Medizintechnik) attached at the end [4]. The applicators were cleaned in an ultrasound bath before each application. For quantifying transmission-related energy losses, the distal applicator power was recorded before and after each application using a power meter (My-Test, Hüttinger Medizintechnik, Munich, Germany). Surgical procedures were performed with a video laparoscopy unit and a complete laparoscopic set of instruments. Sonographic examinations were carried out with high-resolution ultrasound equipment and a 7.5-MHz laparoscopic linear scanner. A flexible nickel-chrome-nickel thermocouple with a diameter of 500 μm (Thermocoax, Philips, Hamburg, Germany) was used to measure tissue temperatures during laser application. The temperature development was recorded every 60 sec via multichannel analyzer. In order to ensure a reproducible distance between thermocouple and applicator, a special holding and introducing device was designed. Using predetermined marks on the holding device, the applicator distances were precisely controlled. Intrahepatic control of the probe position was done by ultrasound.

Surgical Procedures

Twenty German hybrid pigs (weight 18–22 kg, 7–8 weeks old) served as test animals. All experiments were done under inhalation anesthesia following intubation. After induction of a CO_2 pneumoperitoneum, three 10/12 trocars were placed in the upper abdomen. Video optics and the laparoscopic instruments were introduced. The hepatoduodenal ligament was snared for temporary occlusion of liver blood perfusion during laser application. The laser applicators were percutaneously inserted into the abdominal cavity using introduction sheath (Therumo, Japan) (Fig. 1). Their positioning will be described separately for single- and multiple-fiber application (Fig. 2). Each experiment was repeated in ten animals.

Single-fiber application with maintained and interrupted blood perfusion. For single-fiber application with hepatic perfusion, the applicator was introduced into the left liver lobe. The insertion depth of the single-fiber applicator was 20 ± 2 mm. The radial distance from the applicator to the thermocouple was 10 mm, and

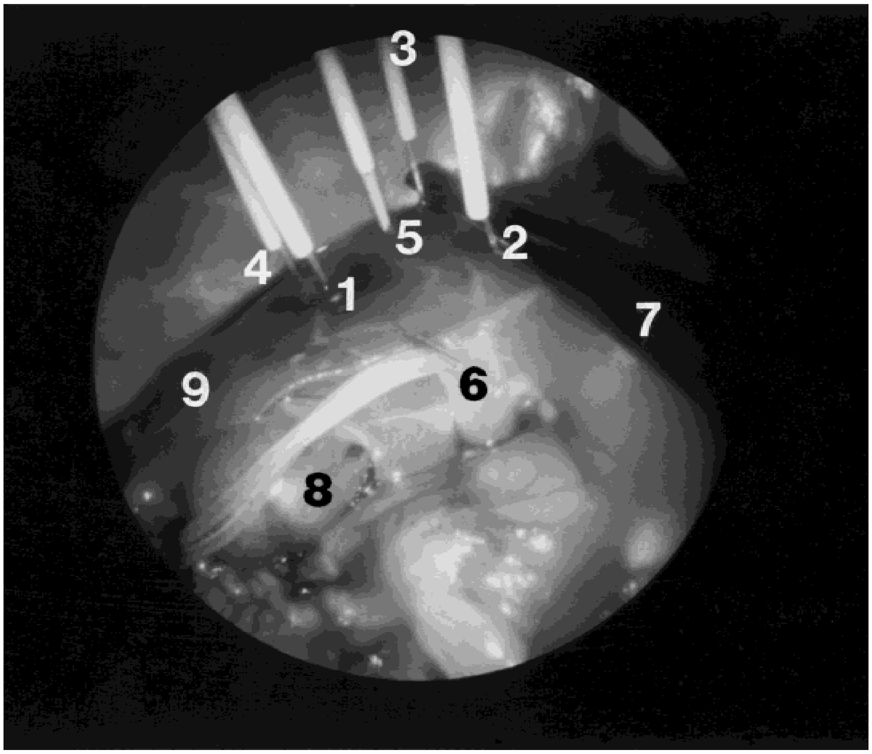

Fig. 1. Intraoperative view during laparoscopy. Laparoscopic ultrasound scanner is placed on the liver surface between applicators. 1–4, Applicators; 5, thermocouple; 6, hepatoduodenal ligament is snared with a silicon loop; 7, ultrasound scanner; 8, gallbladder; 9, liver surface.

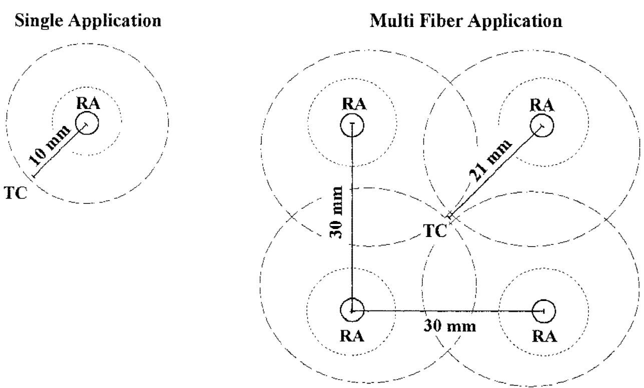

Fig. 2. Graph of the lesions created with hepatic perfusion (dotted line) and during Pringle's maneuver (dashed line). There is no overlapping in multiple-fiber application with hepatic perfusion. RA, Ringmode® applicator; TC, thermocouple.

the insertion depth of the thermocouple was 10 ± 2 mm. Intrahepatic control of the thermocouple and laser applicator position was performed with laparoscopic ultrasound. Laser output was 5 W, exposure time was 840 sec.

After a delay time of about 15 min, placement of the same applicator in the right liver lobe was done for single-fiber application with interrupted hepatic perfusion. Following occlusion of the hepatoduodenal ligament (Pringle's maneuver), the single application with interrupted hepatic perfusion was performed with the same laser parameters. Hepatic blood supply was released approximately 60 sec after completing the laser application; the mean duration of Pringle's maneuver was 900 ± 20 sec.

Multiple-fiber application with maintained and interrupted blood perfusion. Multiple-fiber application was initially performed in the right liver lobe with hepatic perfusion. Therefore, the four applicators were intrahepatically placed under ultrasound guidance in the corners of an imaginary square with an edge length of 30 mm. The insertion depth of the applicators was 20 ± 2 mm. For recording, intrahepatic temperatures in the multiple-fiber application mode, the thermocouple was placed in the center of the square. The insertion depth of the thermocouple was 10 ± 2 mm, and the radial distance from the thermocouple to all applicators was 21 mm. The intrahepatic positions of the thermocouple and the applicators were monitored with laparoscopic ultrasound. Laser output was 30 W, resulting in an output of 5 W at each applicator tip. Exposure time was 840 sec.

After reaching the initial intrahepatic temperature, the applicators and the thermocouple were removed and subsequently placed in the left liver lobe. Multiple-fiber application with interrupted hepatic perfusion was then carried out

with a Pringle maneuver as described for the single-fiber application.

Postoperative Procedures

After completion of treatment, the animals were left under general anesthesia; the applicators and the trocars were removed from the abdominal cavity, and the trocar insertion site was closed. Four hours after the end of laser application, the animals underwent laparotomy for hepatectomy. A 4-hr interval between completing the experiments and removing the liver was chosen in order to ensure a sufficient reperfusion of the liver.

The removed livers were cut vertically to the applicator axis, and the extent of the hyperthermal area was macroscopically measured. Lesion volume was calculated using the formula for the ellipsoid volume $V = 4\pi ab^2/3$, where a is defined as half of the axial and b as half of the radial spread of the lesion. With respect to the applicator characteristics, we assumed that the lesions had a circular symmetric shape.

Relevant histological sections were stained with hematoxylin-eosin or NADH-diaphorase. The latter provided the localization of an active respiratory enzyme, present in all cells.

Statistical Analysis

Mean values and standard errors of the mean (SEM) were calculated from the measured data. The compound t-test was applied to examine differences regarding the individual effects in the entire population or in a subgroup. A variance analysis with measurement repetition allowed the simultaneous study of both effects. The significance level was set at $P < .01$.

RESULTS

Each laser application produced a clearly visible, clay-yellow lesion, which was sharply demarcated from the untreated liver tissue and could be exactly measured.

Maintained Blood Perfusion

In the single-fiber application mode with a total energy of 4,200 J and maintained hepatic perfusion, the mean lesion volume was 2.5 ± 0.5 $cm.^3$. There was a temperature increase to a maximum of 40°C after an application time of 480 sec. No further temperature increase was observed up to the end of application (840 sec). The initial temperature was reached 150 sec after terminating application (Fig. 4).

Multiple-fiber application ($4 \times 4,200$ J) with hepatic perfusion produced four clearly separated tissue lesions with a significantly greater mean individual lesion volume of 3.7 ± 0.5 cm^3 ($P < .01$) (Table 1; Fig. 3). Superposition of the individual lesions in the multiple-fiber mode was never observed with maintained hepatic perfusion. Summation of the individual volumes resulted in a total lesion volume of 14.6 ± 1.3 cm^3 (Table 1; Fig. 3). A maximum temperature increase to 42°C was observed after 600 sec. No further temperature increased occurred up to the end of application (840 sec). The initial temperature was reached 300 sec after the laser had been stopped (Fig. 5).

Interrupted Blood Perfusion

Single-fiber application with a total energy of 4,200 J and temporary interrupted hepatic blood perfusion induced a significantly greater mean lesion volume of 7.5 ± 1.0 cm^3 ($P < .01$) than single-fiber application with maintained blood perfusion, which was 2.5 ± 0.5 cm^3 (Table 1; Fig. 3). Hence, interrupting the hepatic blood flow with a single application increases the necrotic volume by a factor of 3.0. Laser coagulation with interrupted hepatic perfusion in the single-fiber application mode resulted in a statistically higher temperature than single-fiber application with maintained blood perfusion. A temperature maximum of 71°C was obtained after 660 sec (Fig. 4).

Multiple-fiber application with interrupted hepatic blood perfusion led to a significantly larger individual necrotic volume with a mean of 12.6 ± 2.2 cm^3 ($P < .01$) than multiple-fiber application with maintained hepatic blood perfusion, which was 3.7 ± 0.5 cm^3 (Table 1; Fig. 3). The four lesions showed a clear superposition so that a single lesion with a total volume of 50.3 ± 6.6 cm^3 resulted. Interrupting the hepatic blood flow with multiple-fiber application increases the individual necrotic volume by a factor of 3.4. In the multiple-fiber application mode a maximum temperature of 55°C was found after 690 sec. The interval from the end of laser application to the end of Pringle's maneuver was 60 sec, during which time the temperature only slightly decreased to 54°C. After releasing the blood flow, the temperature further decreased to 49°C in the first 20 sec. The initial temperature of 35°C was reached 300 sec after terminating the application (Fig. 5).

The temperature difference between single- and multi-fiber application is a result of the dif-

TABLE 1. Mean Lesion Volume With Maintained (n = 10) and Interrupted Blood Perfusion (n = 10) by Single- (n = 10) and Multiple-Fiber Application (n = 10)

	Single-fiber application			Multiple-fiber application						
	∅ rad. (mm)	∅ axial (mm)	Volume (cm^3)	∅ rad. (mm)	∅ axial (mm)	Volume I (cm^3)	Volume II (cm^3)	Volume III (cm^3)	Volume IV (cm^3)	Volume total (cm^3)
Perfusion	22 (± 1.0)	15 (± 1.3)	2.5 (± 0.5)	22 (± 0.4)	18 (± 0.7)	3.4 (± 0.5)	3.8 (± 0.4)	3.7 (± 0.5)	3.8 (± 0.4)	14.6 (± 1.3)
Occlusion	24 (± 1.3)	25 (± 1.1)	7.5 (± 1.0)	26 (± 1.2)	30 (± 1.5)	12.3 (± 2.1)	12.1 (± 2.8)	12.0 (± 1.5)	13.8 (± 2.0)	50.3 (± 6.6)

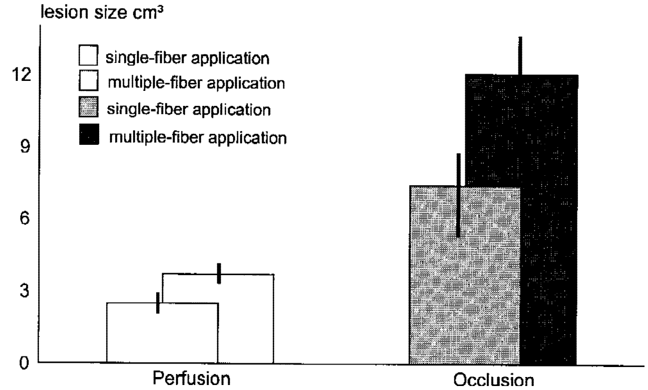

Fig. 3. Influence of application mode and hepatic perfusion on inducible lesion volume. Resulting mean single lesion volumes are specified.

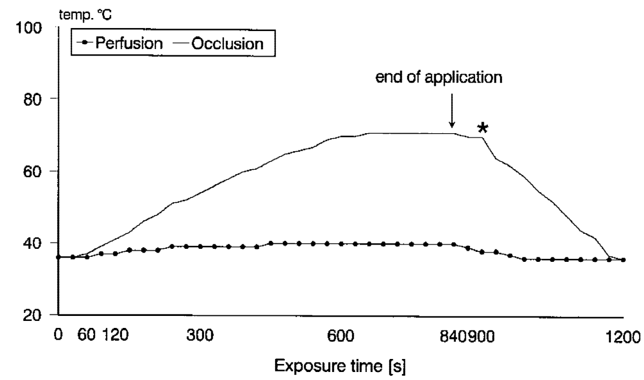

Fig. 4. Course of intrahepatic temperatures in single-fiber application with preservation (Perfusion) and temporary interruption of hepatic perfusion (Occlusion). Asterisk: Release of Pringle's maneuver, distance between thermocouple and applicator was 10 mm.

ferent distances between fiber(s) and thermocouple which was 10 mm in single-fiber application and 21 mm in multi-fiber application (Fig. 2).

Histology

In HE staining the cells in the area of laser coagulation showed the typical signs of acute thermal damage such as cell shrinkage and hyperchromasia [17]. The NADH-diaphorase stain showed that cell damage was less pronounced in areas surrounding larger vessels when hepatic perfusion was preserved (Fig. 6). Without perfusion no difference in the degree of cell damage was found in the proximity of larger vessels. In addition, the coagulated areas induced with preserved hepatic perfusion showed vacuoles in the extracellular space in the immediate vicinity of the applicator ("popcorn" effect) [17]. In the lesions induced during interrupted hepatic perfusion, the

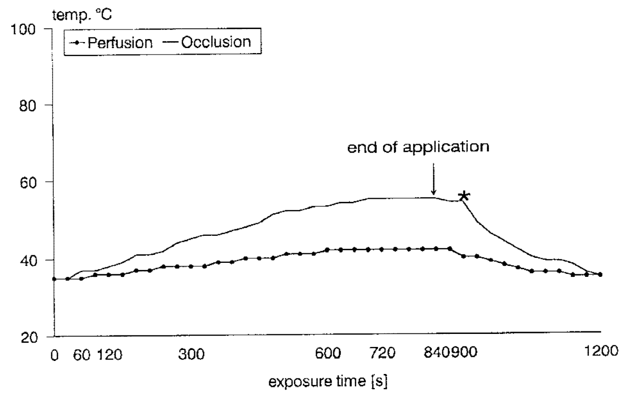

Fig. 5. Course of intrahepatic temperatures in multiple-fiber application with preservation (Perfusion) and temporary interruption of hepatic perfusion (Occlusion). Asterisk: Release of Pringle's maneuver, distance between thermocouple was applicator 21 mm.

vacuoles were more widely scattered and located more distant to the applicator. The typical signs of thermic cell damage were seen in the macroscopically visible superposition zone between two lesions created by multiple-fiber application during interrupted hepatic perfusion. Such signs were not detected in the transition zones with preserved hepatic perfusion. Carbonization around the applicator zone was not found in any of the cases.

DISCUSSION

According to the cascade theory of metastatic spread, curative treatment of primary as well as secondary liver tumors by local therapy is useful only in patients with tumors limited exclusively to the liver [18,19]. At present, the only therapeutic procedure with a potentially curative objective is liver resection with a statistical 5-year survival rate of 30% [20]. However, taking prognostically relevant factors into account, only a maximum of 30% of the affected patients can be considered for liver surgery [20–22]. Interstitial laser coagulation (ILC) is a novel therapeutic procedure for the treatment of malignant liver tumors [1]. However, the useful clinical application of ILC is still limited by the small size of inducible tumor destruction (coagulation lesions) with a single application.

The size of the induced necrosis area is dependent on different factors such as laser parameters (laser power/exposure time), the application system (bare fiber/diffusing fiber tip) and the application mode (multiple/single-fiber application) as well as on optical and physiological properties of the treated tissue [8,9,11,23,24]. The aim of this experimental study was to investigate the effect of hepatic perfusion on coagulation volume in single- and multiple-fiber application. In this animal model, laparoscopic single- and multiple-fiber applications were performed with maintained hepatic perfusion as well as occlusion of the hepatoduodenal ligament (Pringle's maneuver).

The results showed that a significantly smaller lesion volume of 2.5 ± 0.5 cm^3 was induced by single-fiber application with maintained hepatic perfusion compared to the individual lesion by multiple-fiber application (3.7 ± 0.5 cm^3). This effect can be explained by heat accumulation between the applicators of the multiple-fiber application system. Whereas two tissue lesions are formed by consecutive irradiation of two adjacent targets (time sharing), simultaneous irradiation (energy sharing) leads to the formation of an additional "hyperthermic bridge" [25]. This synergistic interaction of the individual heat foci results in a superadditive effect that increases the efficiency of the transmitted laser energy. Consequently, larger tissue necroses are produced in the energy-sharing multiple-fiber application mode. In an experimental study, Steger et al. used a multiple-fiber application system which allowed the simultaneous application of four bare quartz fibers. In the study design, a laser fiber distance of 15 mm was chosen, and blood perfusion was maintained. A total energy of 4,020 J resulted in a total lesion volume of 10 cm^3 with superposition of the individual lesions [11].

In contrast to the results of Steger et al., our own experiments with a multiple-fiber application system (fiber distance 30 mm) and an applied laser energy of $4 \times 4{,}200$ J (5 W/840 sec) resulted in four individual tissue lesions of 3.7 cm^3. Summation of the four individual lesions yielded a total volume of 14.6 cm^3. The fact that the individual lesions did not overlap with preserved hepatic perfusion can be explained by the 30-mm applicator distance. Under the selected conditions, the superposition of temperature fields increased the size of the individual lesions, but the coagulation threshold was not reached between the applicators. Svaasand et al. described hepatic perfusion as the main cause of reduced temperature development and thus smaller hyperthermic lesions. Depending on blood flow rate and vessel diameter, there is a cooling effect due to efferent heat conduction [10]. In animal experiments, Matthewson et al. found areas of markedly less

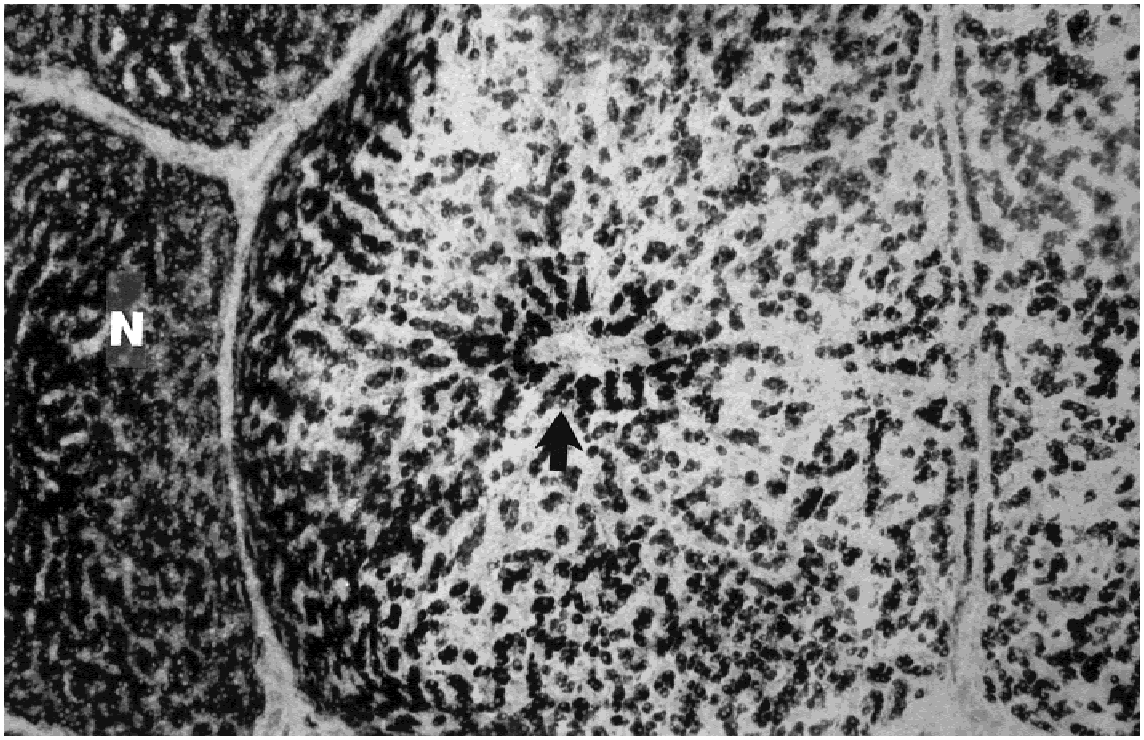

Fig. 6. NADH-diaphorase stain. Maintained blood perfusion: less-pronounced cell damage in areas surrounding large vessels.

pronounced tissue damage in laser-induced coagulation necroses surrounding larger intrahepatic vessels [16]. Our own results showed the same histopathological changes in lesions created with maintained hepatic perfusion.

Temporary interruption of hepatic blood flow by occluding the hepatoduodenal ligament can be considered as a safe procedure for an interval of 50–60 minutes because of the known normothermic period of liver ischemia [26]. The results show that the cooling effect of hepatic perfusion can be eliminated under laparoscopic conditions using the so-called Pringle's maneuver during laser application. Correspondingly, Sweetland et al. found a temperature increase of 1–2°C during interstitial laser hyperthermia (2 and 3 W/400 sec) due to temporary ischemia of rat liver lobes compared to application with normal perfusion [27].

Our investigations show that the volume of tissue lesions induced with interrupted hepatic blood flow in the single application mode was significantly larger by a factor of 3.0 than the lesions created during hepatic perfusion. Analogous to single applications, the multiple-fiber applications with temporary interruption of hepatic circulation yielded significantly greater lesion volumes by a factor of 3.4. In all laser applications performed with Pringle's maneuver, there was an overlapping of the individual lesions, resulting in a hyperthermally induced area with a total volume of 50.3 cm^3.

The significance of our results is limited by the fact that they were obtained in healthy, homogeneously perfused liver and not in liver tumors. On the other hand, it is known from studies on the surgical resection of liver metastases that a safety zone of 1 cm of peritumorous healthy liver tissue is required for complete tumor removal [21,28]. The basic oncological principles for surgical resection must also apply to the clinical use of interstitial laser coagulation as an in situ ablation technique. Various animal experimental studies showed that a maximal lesion diameter of 25–30 mm can be obtained by using specially developed application systems under physiological conditions [8,11,23,29]. Thus, with a required safety zone of 1 cm, only tumors with a maximum diameter of 1 cm could be safely treated with ILC. For the clinical treatment of human liver tumors larger lesion volumes are required in the majority of cases. In conclusion, our results clearly demonstrated that a significant increase in lesion volume can be obtained with temporary occlusion of the hepatoduodenal ligament during laser application. An additional increase in the coagulated

volume can also be achieved by using a multiple-fiber application system.

The results of this study showed that interstitial laser coagulation as an in situ ablation technique for treating malignant liver tumors should preferably be performed via application routes that permit temporary interruption of hepatic perfusion. Thus, the laparoscopic access seems best suited, as it allows both a multiple-fiber application and performance of Pringle's maneuver to eliminate the cooling effect through the temporary interruption of hepatic perfusion.

REFERENCES

1. Bown SG. Phototherapy of tumors. World J Surg 1983; 7:700–709.
2. Amin Z, Bown SG, Lees WR. Local treatment of colorectal liver metastases: a comparison of interstitial laser photocoagulation (ILP) and percutaneous alcohol injection (PAI). Clin Radiol 1993; 48:166–171.
3. Vogl TJ, Müller PK, Hammerstingl R, Weinhold N, Mack MG, Philipp C, Deimling M, Beuthan J, Pegios W, Reiss H, Lemmens HP, Felix R. Malignant liver tumors treated with MR imaging-guided laser-induced thermotherapy: Technique and prospective results. Radiology 1995; 196: 257–265.
4. Germer CT, Albrecht D, Roggan A, Isbert C, Buhr HJ. An experimental study of laparoscopic laser-induced thermotherapy treatment for liver tumors. Br J Surg 1997; 84: 317–320.
5. Nolsoe CP, Torp-Pedersen S, Burcharth F, Horn T, Pedersen S, Christensen NEH, Olldag ES, Andersen PH, Karstrup S, Lorentzen T, Holm HH. Interstitial hyperthermia of colorectal liver metastases with a us-guided Nd-YAG laser with a diffuser tip: a pilot clinical study. Radiology 1993; 187:333–337.
6. Schneider PD. Liver resection and laser hyperthermia. Surg Clin North Am 1992; 72:623–632.
7. Ravikumar TS. Interstitial therapies for liver tumors. Surg Oncol Clin North Am 1996; 2:365–377.
8. Wyman DR, Whelan WM, Wilson DC. Interstitial laser photocoagulation: Nd:YAG 1064 nm optical fibersource compared to point heat source. Lasers Surg Med 1992; 12:659–664.
9. Van Hillegersberg R, van Steveren HJ, Kort WJ, Zondervan PE, Terpstra OT. Interstitial Nd:YAG laser coagulation with a cylindrical diffusing fiber tip in experimental liver metastases. Lasers Surg Med 1994; 14:124–133.
10. Svaasand LO, Gomer CJ, Morinelli E. On the physical rationale of laser induced hyperthermia. Lasers Med Sci 1990; 5:121–127.
11. Steger AC, Lees WR, Shorovon P, Walmsley K, Bown SG. Multiple-fiber low-power interstitial laser hyperthermia: studies in the normal liver. Br J Surg 1992; 79:139–145.
12. Wyman DR, Whelan WM. Basic optothermal diffusion theory for interstitial laser photocoagulation. Med Phys 1994; 21:1651–1656.
13. Bowman HF. Estimation of tissue blood flow. In: Shitzer A, Eberhart RC, eds. "Heat Transfer in Medicine and Biology." New York: Plenum Press 1985, pp 193–226.
14. Roemer RR. Thermal Dosimetry. In: Gauthiere M, ed. "Thermal Dosimetry and Treatment Planing." New York: Springer, 1990, pp 119–210.
15. Arkin DA, Tannehill JC, Pletcher RH. Computational fluid mechanics and heat transfer. New York: McGraw-Hill, 1984.
16. Matthewson K, Coleridge-Smith P, O'Sulivan JP, Northfield TC, Bown SG. Biological effects of intrahepatic neodymium: yttrium-aluminium-garnet laser photocoagulation in rats. Gastroenterology 1987; 93:550–557.
17. Thomsen S. Pathologic analysis of photothermal and photomechanical effects of laser-tissue interactions. Photochem Photobiol 1991; 53:825–835.
18. Taylor I. Liver metastases from colorectal cancer: lessons from past and present clinical studies. Br J Surg 1996; 83:456–460.
19. Murphy P, Alexander P, Senior PV, Fleming J, Kirkham N, Taylor I. Mechanisms of organ selective tumour growth by bloodborne cancer cells. Br J Cancer 1988; 57: 19–31.
20. Hughes K, Simon R, Adson MA. Registry of hepatic metastases: resection of the liver for colorectal carcinoma metastases—a multi-institutional study of indications for resection. Surgery 1988; 103:278–288.
21. Scheele J, Stangl R, Altendorf-Hofmann A, Paul M. Resection of colorectal liver metastases. World J Surg 1995; 19:59–71.
22. Adson MA, van Heerden JA, Adson MH, Wagner JS, Ilstrup DM. Resection of hepatic metastases from colorectal cancer. Arch Surg 1984; 119:647–651.
23. Albrecht D, Germer CT, Foss HD, Roggan A, Häring R. Laserinduzierte Thermotherapie (LITT) zur Behandlung maligner Lebertumoren—Ex-vivo Studie zur Applikatorerprobung Langenbecks Arch Chir 1994; 278–282.
24. Roggan A, Dörschel K, Minet O, Wolff D, Müller G. Optical properties of biological tissues in the near-infrared wavelength range: review and measurements. In: Müller G, Roggan A, eds. "Laser-Induced Interstitial Thermotherapy." Washington, SPIE 1995, pp 224–248.
25. Frank F, Hessel S. Technical prerequisites for the interstitial thermotherapy with the Nd: YAG laser. Lasermedizin 1990; 1:36–40.
26. Huguet C, Nordlinger B, Bloch P, Conard J. Tolerance of the human liver to prolonged normothermic ischemia: a biologic study of 20 patients submitted to extensive hepatectomy. Arch Surg 1978; 113:1448–1455.
27. Sweetland HM, Wyman A, Pogers K. Evaluation of the effect on normal liver of interstitial laser hyperthermia using artificial sapphire probes. Lasers Med Sci 1993; 8:99–105.
28. Cady B, Stone MD, McDermott WV, Jenkins RL, Bothe A, Lavin PT, Lovett EJ, Steele GD. Technical and biological factors in disease-free survival after hepatic resection for colorectal cancer metastases. Arch Surg 1992; 127:561–569.
29. Malone DB, Wyman DR, Moote DJ, DeNardi FG, Mori H, Swift C, Lewis R, Stevenson GW, Wilson BC. Sonographic changes during hepatic interstitial laser photocoagulation: an investigation of three optical fiber tips. Invest Radiol 1992; 27:804–813.